alleges that the specification "fails to provide support for a claim drawn to a monoclonal antibody having the highly restricted binding specificity of that claimed in claim 12, wherein the antibody is a human antibody produced by a lymphocyte isolated from an individual with prostatic carcinoma." According to the Examiner, it is not clear that one of ordinary skill in the art could produce the claimed invention, "[g]iven the high degree of unpredictability of successfully establishing stable cell lines producing human monoclonal antibodies . . . and the lack of exemplary material demonstrating the feasibility of producing such a cell line." Claim 15 has been canceled, thereby obviating the objection and rejection.

Claims 1-23 and 28-30 stand rejected under 35 U.S.C. §112, first paragraph. The Examiner asserts that the disclosure is enabling "only for claims limited to the monoclonal antibody and cell line 7E11C and methods for its production and use, which are exemplified in the specification." Given that the specification discloses a single example of a cell line which produces a monoclonal antibody having the claimed properties and the "unpredictability of producing further cell lines having the claimed properties," Examiner Hutzell does not believe that one of ordinary skill in the art could produce further cell lines and antibodies having the claimed properties "based on the written specification alone."

Claims 1-6 and 28-30, as now amended, are more specifically directed to cell line 7E11-C5, thereby obviating the objection and rejection with respect to these claims. With respect to claims 16-19, applicant points out that there is no evidence of record that anyone had previously utilized LNCaP cells alone to successfully immunize mice for the purpose of creating the described lymphocytes. The process for producing monoclonal antibodies, starting with the step of immunizing mice

with LNCaP cells is clearly enabled by the present specification, particularly Figure 1 and the description at pages 24-31.

Examiner Hutzell maintains the objection to the specification, and the rejection of claims 1-24, 26, and 28-31, under 35 U.S.C. §112, first paragraph, stating that while the previously submitted Declaration appears to be sufficient to overcome the rejection, there appears to be a discrepancy between the designation of the cell line in the deposit conversion document and that disclosed in the specification. The Examiner specifically has requested that applicant "clarify the relationship between 7E11C5 cell line identified in the ATCC document and the 7E11C cell line described in the specification."

Two exhibits were appended to the Declaration of S. Leslie Misrock, submitted September 4, 1990. Included among the documents comprising Exhibit A were two letters from Pennie & Edmonds to the American Type Culture Collection, and an ATCC form for making a deposit under the Budapest Treaty. Each of these three documents correctly identifies the cell line being deposited as having the Strain Designation 7E11C5. As is clear, however, from the other document comprising Exhibit A, ATCC Form BP4/9, the ATCC, in transcribing the information from one form to another, omitted part of the strain designation. Unfortunately, the Declaration of S. Leslie Misrock, submitted September 4, 1990, carried forward the incorrect designation. Accordingly, a Supplemental Declaration of S. Leslie Misrock is submitted herewith which states that the material deposited with the ATCC is, indeed, the same as the 7E11-C5 hybridoma cell line referenced in the captioned application. In light of this Supplemental Declaration, the objection and rejection should be withdrawn.

Claims 1-3, 10, 11, 20, 28, 29, and 31, remain rejected under 35 U.S.C. 102(b)/103 over Frankel et al. for reasons of

record. In the Office Action dated March 1, 1990 (Paper No. 3), the Examiner concluded that the claimed cell lines and monoclonal antibodies would have been anticipated or rendered *prima facie* obvious by Frankel's teaching of mouse monoclonal antibodies which are specific for membrane-associated antigens present on human prostatic cancer and normal prostatic epithelium. Applicant, in an Amendment filed September 4, 1990, pointed out that the Frankel monoclonal antibodies exhibited considerable cross-reactivity with respect to other tissues. Examiner Hutzell now indicates that these arguments were not persuasive because the claims are not limited to antibodies which lack cross-reactivity to these tissues, "but are broadly drawn to monoclonal antibodies specific for a membrane-associated prostate epithelium-specific antigen. . ."

Claims 1-6, 28, 29, and 31, as now amended, are specifically drawn to monoclonal antibodies which do not cross-react with non-prostatic antigens present in other tissues, and thus do not read on the monoclonal antibodies disclosed in Frankel. Claims 10, 11, and 20, have been canceled. This rejection, therefore, is no longer proper and should be withdrawn.

Claims 1-6, 10-14, 20-22, 28, 29, and 31, remain rejected, and claim 23 is rejected, under 35 U.S.C. 102(b)/103 over Finstad et al for reasons of record. In the Office Action dated March 1, 1990 (Paper No. 3), the Examiner noted that Finstad describes a mouse monoclonal antibody "with a specificity for a membrane-associated antigen present on normal and malignant human prostate epithelium." Applicant, in an Amendment filed September 4, 1990, noted that the Finstad monoclonal antibodies exhibited considerable cross-reactivity with respect to other tissues. Examiner Hutzell now indicates that these arguments were not persuasive because the claims are not limited to antibodies which lack cross-reactivity to these tissues.

Claims 1-6, 28, 29, and 31, as now amended, are specifically drawn to monoclonal antibodies which do not cross-react with non-prostatic antigens present in other tissues, and thus do not read on the monoclonal antibodies disclosed in Finstad. The remaining claims subject to this rejection have been canceled. This rejection, therefore, is no longer proper and should be withdrawn.

Claims 1-3, 5, 7-11, 28, 29, and 31, remain rejected under 35 U.S.C. §102(b)/103 over Webb et al. In response to applicant's prior argument that the Webb monoclonal antibodies cross-reacted with liver, trachea, tonsil, etc., Examiner Hutzell now indicates that the claims are not limited to antibodies which lack cross-reactivity with these tissues. Claims 1-3, 5, 28, 29, and 31, as now amended, are specifically drawn to monoclonal antibodies which do not cross-react with non-prostatic antigens present in other tissues, and thus do not read on the monoclonal antibodies disclosed in Webb. Claims 7-11 have been canceled. This rejection, therefore, is no longer proper and should be withdrawn.

Examiner Hutzell further maintains the rejection of claims 16, 17, and 19, under 35 U.S.C. §103 over Webb et al., stating that "[e]ven if the claimed antibodies and hybridomas are distinguished over the prior art of record, the claimed processes for producing monoclonal antibodies are conventional and obvious over the prior art in the absence of evidence establishing the unobviousness of applying the conventional methods for the production of the claimed antibodies and hybridomas."

As explained above, claim 16 is specifically directed to a process utilizing LNCaP cells or fractions to obtain cells capable of producing the monoclonal antibodies of the invention. There is no evidence of record that anyone had previously utilized LNCaP cells alone to ultimately obtain the monoclonal

antibodies with the recited specificities and reactivities. Nothing in Webb suggests that one should use the LNCaP cells in the claimed process to produce monoclonal antibodies which are specific for normal and malignant prostate epithelium, and which do not cross-react with non-prostatic antigens in other tissues. Therefore, these claims are not obvious over the cited art and the rejection should be withdrawn.

Claims 1-3, 5-11, 16-20, 22, and 28-31 remain rejected under 35 U.S.C. §103, as obvious over Campbell et al. in view of Frankel et al., or Webb et al., or Wright et al. Claims 7-11 and 20 have been canceled. With respect to claims 1-3, 5-6, and 28-31, applicant submits, that for all of the reasons already argued --particularly the change of the present claims to recite monoclonal antibodies produced by a specific hybridoma, which have very specific reactivities-- the cited references do render the claimed invention obvious. With respect to claims 16-19, applicant reiterates that the utilization of LNCaP cells renders the claimed processes non-obvious.

Applicant submits that the case is now in condition for allowance. An early Notice of Allowability is earnestly solicited.

Respectfully submitted,

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